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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,411	12/07/2000	Samy Ashkar	CMZ-124CP	1508

7590 04/22/2003

PATREA L. PABST
HOLLAND & KNIGHT LLP
2000 ONE ATLANTIC CENTER
1201 WEST PEACHTREE STREET, SUITE 2000
ATLANTA, GA 30309-3400

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/22/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/732,411	ASHKAR, SAMY
Examiner	**Art Unit**
Maher M. Haddad	1644

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *2,6,9,10,14 and 20-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 5, 7-8, 11-13 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4)☐ Interview Summary (PTO-413) Paper No(s) _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 2 21 03 (Paper No. 14), is acknowledged.

2. Claims 1-29 are pending.

3. Claims 2, 6, 9-10, 14 and 20-29 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 1, 3, 4, 5, 7-8, 11-13 and 15-19 are under examination as they read on a method of inhibiting decreasing adhesion of a target cell to a substrate comprising providding the target cell with the adhesion modulatory peptided associated substrate of SEQ ID NO:15 (inhibits VLA-4 VCAM interaction) such that adhesion of the target cell to the substrate is inhibited wherein the target cell is endothelial cells, neutrophil and macrophage and wherein the substrate is titanium, a polyvinyl surface, a gel, collagen, hyaluronic acid and PGA.

5. In view of the amendment filed on 2-21-03, only the following rejections are remained.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-5, 7-8, 11-13 and 15-19 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting adhesion of a target cell to a substrate *in vitro*, comprising providing the target cell with the adhesion peptide SEQ ID NO: 1-15 and SDV associated substrate, wherein the target cell is an endothelial, a macrophage or neutrophil and the substrate is a polyvinyl surface, a gel, collagen, hyaluronic acid, titanium and PGA, does not reasonably provide **enablement** for a method for enhancing or decreasing adhesion of a target cell to a substrate comprising providing the target cell with any "adhesion modulatory peptide"-associated substrate such that adhesion of the target cell to the substrate is enhanced or decreased as compared to substrate alone, wherein the target cell expresses a receptor selected from the group consisting of $\alpha 4\beta 1$ integrins and VCAMs, wherein the peptide binds to the receptors in claim 1, wherein the adhesion modulatory peptide comprises any peptide which specifically inhibits adhesion of the target cell in claim 3, wherein the adhesion modulator peptide is any "endothelial cell adhesion modulator peptide" any "fibroblast adhesion modulatory peptide" or any "macrophage adhesion modulatory peptide" in clam 4, wherein the adhesion modulatory peptide is any "endothelial cell adhesion modulatory peptide" in claim 5, wherein the adhesion modulatory peptide is any "neutrophil adhesion modulatory peptide" or any "myofibroblast adhesion modulatory peptide' in claim 7, wherein the "adhesion modulatory molecule" inhibits binding of any "adhesion receptor predominantly" expressed by the target cell in claim 11, wherein the target cell is within a "subject" in claim 17, the method further

comprising contacting the substrate with the adhesion modulatory peptide, forming the adhesion modulatory peptide-associated substrate prior to providing the cell with the substrate in claim 19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim essentially for the same reasons set forth in the previous Office Action, paper No. 11, mailed 11 18 02.

Applicant's arguments, filed 2 21 03 (Paper No. 14), have been fully considered, but have not been found convincing.

Applicant requests clarification as to how a myriad of indirect effects associated with adhesion pathways, has bearing on issues related to an enabling disclosure for claims directed to extracellular interactions.

Since any peptide that effect the adhesion can act indirectly by effecting (positively or negatively) the production of cytokines for example. The specification is not enabled for such peptides.

Applicant asserts that one skilled in the art will recognize that structure of a peptide/ligand is defined by the receptor to which it interacts. Further, applicant argues that Kogan et al teachings of mutagenic analysis (i.e. "wrecking") and the subsequent assaying of binding (i.e. "checking"), was done to merely prove, or disprove, a proposed model of binding. Applicant further asserts in conjunction how the state-of-the art in pharmaceutical designing peptide that one a suitable receptor directed ligand is found, amino acid residues in the optimal substrate are deleted/substituted with other moieties to find the optimal inhibitors. Applicant further argues that the receptor(s) of interest define the claimed peptides both structurally and functionally.

Contrary to Applicant's assertions, Kogan et al teach that single amino acid can determine the ligand specificity of a selectin and the unpredictable nature of amino acid alterations in adhesion binding activity. Further, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 1-15 is essential for maintain its inhibitory activity and which changes can be made in the structure of SEQ ID NO: 1-15 and still maintained the same function. Further, the enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NO:15 would have been altered such that the resultant polypeptide would have retained the function of inhibiting the interaction between VLA-4 and VCAM interaction. Furthermore, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and or use the invention, not how delete substitute to identify the invention. Until the time when peptides are found, then one skill in the art can make them.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

11. Claims 1, 3-5, 7-8, 11-13 and 15-19 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, paper No. 11, mailed 11/18/02.

Applicant's arguments, filed 2/21/03 (Paper No. 14), have been fully considered, but have not been found convincing.

Applicant argues in conjunction with law cases that an adequate written description is achieved by (1) the structural and functional properties of claimed peptides, (2) the amended claims no longer encompass "any adhesion modulator peptide".

However, there is no described or art-recognized correlation or relationship between the structure of the invention, the SEQ ID NO: 15 and it's inhibition of VLA4/VCAM interaction function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of adhesion modulator peptide-associated substrate comprising a peptide, which specifically inhibits adhesion of target cell.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 4-5, 12, 13, 16, and 18-19 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S Patent No. 5,330,911 for the same reasons set forth in the previous Office Action, paper No. 11, mailed 11/18/02.

The '911 patent teaches a method of modulating enhancing adhesion of a target cell to a substrate, comprising providing the target cell with a peptide grafted surfaces or YIGSR-linked substrates such that the target cell to the substrate is attached, indicating that cellular adhesion on these substrates is governed primarily by cell receptor-ligand interactions (abstract and column 5, line 24-39 and column 30, lines 33-37 in particular), wherein the cell is endothelial cells (column 6, lines 6-7 in particular), wherein the substrate is titanium (column 46, lines 15-16 in particular).

Further, the '911 patent teaches the pretreatment of surfaces with a peptide prior to providing the endothelial cells with the substrate (see patented claim 45 in particular) as recited in instant claim 19.
The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 2-21-03 (Paper No. 14), have been fully considered, but have not been found convincing.

Applicant argues that the '911 patent teaches the inhibition of cell spreading on RGD and YIGSR peptide-grafted surfaces due to the presence of soluble peptide in the surrounding medium. Applicant further argues that the '911 patent does not teach or contemplate a peptide whose structure is inherently predicted on the binding motifs of $\alpha 4\beta 1$ integrins and or VCAM receptors expressed on by the target cell.

Contrary to applicant assertions, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which a particular complex of one or more receptor(s) and a ligand is inhibited enhanced does not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same end result. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

13. The following new ground of rejection is necessitated by the amendment filed on 2-21-03, paper No. 14.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

15. Claims 1, 3-5, 7-8, 11-13 and 15-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "as compared to substrate alone, wherein the target cell expresses a receptor selected from the group consisting of $\alpha 4\beta 1$ integrins and VCAMs, wherein the peptide binds to the receptors" claimed in claim 1, lines 5-6 represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 2/21/03 points to the specification at page 2, lines 25-29, page 3, lines 1-2 and page 4, lines 1-9 for support for the newly added limitations "as compared to substrate alone, wherein the target cell expresses a receptor selected from the group consisting of $\alpha 4\beta 1$ integrins and VCAMs, wherein the peptide binds to the receptors" as claimed in claim 1. However, the specification does not provide a clear support of "as compared to substrate alone, wherein the target cell expresses a receptor selected from the group consisting of $\alpha 4\beta 1$ integrins and VCAMs, wherein the peptide binds to the receptors". The instant claims now recite limitations which were not clearly disclosed in the specification and claims as originally filed.

16. No claim allowed

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
April 18, 2003

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600